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agent effective to alter the proliferation or growth of the lung cancer cells, wherein the agent is selected from a heagehog antagonist, a ptc agonist, and an fgf-10 antagonist.

2. (Twice Amended) A method for inhibiting the growth of a lung tumor which expresses hedgehog, comprising contacting the lung tumor with an amount of an agent effective to inhibit the growth of the lung tumor, wherein the agent is selected from a hedgehog antagonist, a ptc agonist, and an fgf-10 antagonist.

3. (Amended) The method of claim 1, wherein the lung cancer tissue is in culture, and the agent is provided as a cell culture additive.

- 4. (Reiterated) The method of claim 1, wherein the cell is treated in an animal and the agent is administered to the animal as a therapeutic composition.
- 5. (Twice Amended) The method of claim 1 or 2, wherein the agent is a hedgehog antagonist.
- 6. (Reiterated) The method of claim 5, wherein the *hedgehog* antagonist is a polypeptide including a *hedgehog* polypeptide sequence of at least an extracellular portion of a *hedgehog* polypeptide that binds to a *patched* polypeptide and blocks *hedgehog* signaling.
- 7. (Reiterated) The method of claim 6, wherein the polypeptide includes at least 50 amino acid residues of an N-terminal half of the hedgehog polypeptide.
- 8. (Reiterated) The method of claims 6, wherein the polypeptide includes at least 100 amino acids of an extracellular domain of the hedgehog polypeptide.
- 9. (Reiterated) The method of claim 6, wherein the polypeptide includes at least a portion of the hedgehog polypeptide corresponding to a 19 kd fragment of an extracellular domain of the hedgehog polypeptide.

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- 10. (Reit rated) The method of claim 6, wherein the hedgehog polypeptide is encoded by a nucleic acid of a vertebrate organism.
- 11. (Reiterated) The method of claim 6, wherein the polypeptide includes a hedgehog polypeptide sequence represented in the general formula of SEQ ID No: 21.
- 12. (Reiterated) The method of claim 6, wherein the polypeptide includes a hedgehog polypeptide sequence represented in the general formula of SEQ ID No: 22.
- 13. (Reiterated) The method of claim 6, wherein the hedgehog polypeptide is encoded by a human hedgehog nucleic acid.
- 14. (Reiterated) The method of claim 6, wherein the hedgehog polypeptide sequence is at least 60 percent identical to an amino acid sequence of a hedgehog protein selected from SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15 SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.
- 15. (Reiterated) The method of claim 6, wherein the hedgehog polypeptide sequence is encodable by a nucleic acid sequence which hybridizes under stringent conditions, including a wash step of 2.0X SSC at 50 °C, to a sequence selected from SEQ ID No:1, SEQ ID No:2, SEQ ID No:3, SEQ ID No:4, SEQ ID No:5, SEQ ID No:6, SEQ ID No:7, SEQ ID No:8, SEQ ID No:9, and SEQ ID No:19.
- 22. (Reiterated) The method of claim 1 or 2, wherein the hedgehog antagonist, patched agonist, or fgf-10 antagonist is a small organic molecule.
- 23. (Reiterated) The method of claim 5, wherein the *hedgehog* antagonist is a small organic molecule.
- 24. (Reiterated) The method of claim 5, further comprising preparing a formulation including an identified *hedgehog* antagonist and a pharmaceutically acceptable excipient.

- 25. (Reiterated) The method of claim 5, wherein the hedgehog antagonist binds to hedgehog and blocks hedgehog signal transduction.
- 26. (Reiterated) The method of claim 5, wherein the binding of the hedgehog antagonist prevents the upregulation of patched and/or gli expression.
- 27. (Reiterated) The method of claim 5, wherein the hedgehog antagonist decreases hedgehog signal transduction by altering the localization, protein-protein binding and/or enzymatic activity of an intracellular protein involved in a hedgehog signal transduction pathway.
- 28. (Reiterated) The method of claim 5, wherein the hedgehog antagonist alters the level of expression of a hedgehog protein, a patched protein or a protein involved in a hedgehog signal transduction pathway.
- 29. (Reiterated) The method of claim 6, wherein the *hedgehog* polypeptide sequence is at least 75 percent identical to an amino acid sequence of a *hedgehog* protein selected from SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.
- 30. (Reiterated) The method of claim 6, wherein the *hedgehog* polypeptide sequence is at least 85 percent identical to an amino acid sequence of a *hedgehog* protein selected from SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.
- 31. (Reiterated) The method of claim 6, wherein the *hedgehog* polypeptide sequence is at least 90 percent identical to an amino acid sequence of a *hedgehog* protein selected from SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.
- 32. (Reiterated) The method of claim 6, wherein the hedgehog polypeptide sequence is at least 95 percent identical to an amino acid sequence of a hedgehog protein selected from SEQ ID

No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.

The amended claims are restated below to reflect changes from the last filing.

- 1. (Twice Amended) A method for [modulating]inhibiting at least one of the proliferation[, differentiation, or] and growth [survival] of lung cancer cells [tissue] which express hedgehog [or cells derived therefrom], comprising contacting the cells [tissue] with an amount of an agent effective to alter the proliferation[, differentiation,] or growth [survival] of the lung cancer cells [tissue], wherein the agent is selected from a hedgehog antagonist, a ptc agonist, and an fgf-10 antagonist.
- 2. (Twice Amended) A method for [inducing the formation of, or the maintenance or functional performance] inhibiting the growth of a lung tumor which expresses hedgehog [tissue], comprising contacting the lung tumor [tissue] with an amount of an agent effective to [induce the formation of new] inhibit the growth of the lung [tissue] tumor, wherein the agent is selected from a hedgehog antagonist, a ptc agonist, and an fgf-10 antagonist.
- 3. (Amended) The method of claim 1, wherein the lung <u>cancer</u> tissue is in culture, and the agent is provided as a cell culture additive.
- 5. (Twice Amended) The method of claim 1 or 2, wherein the agent is a hedgehog antagonist.

## **REMARKS**

Claims 1-32 constitute the pending claims in the present application. Claims 1-17 and 22-32 were elected with traverse. Applicants will cancel non-elected claims upon indication of allowable subject matter. Applicants cancel, without prejudice, claims 16 and 17. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the